Journal of the Neurological Sciences 475 (2025) 123589

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Clinical short communication

Neuromyelitis Optica Spectrum disorder – Clinical profile, treatment and risk factors for relapse in three tertiary hospitals in South Africa. An observational study

Jerry George *, Eitzaz Sadiq, Andre Mochan

Division of Neurology, Department of Neurosciences, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

ARTICLE INFO

Keywords:
Neuromyelitis optica
Relapses
Chronic immunosuppression
Africa
HIV
Rituximab

ABSTRACT

Introduction: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory syndrome characterised by Aquaporin-4 antibodies (AQP4 Ab). Clinical presentations include optic neuritis, longitudinally extensive transverse myelitis (LETM), area postrema syndrome, diencephalic and cerebral syndromes. Immunosuppressants are used to prevent relapses and disability. There is little data from sub-Saharan Africa on the clinical presentations and outcomes of patients with NMOSD.

Methods: An observational study was conducted between January 2023 and June 2024 at three hospitals in Johannesburg, South Africa. We included all patients with NMOSD who had a minimum of 12 months follow up after diagnosis. Data was collected on demographics, clinical manifestations, AQP4 Ab status, immunosuppressive medications used, and relapses.

Results: Thirty-nine patients were recruited, all black African; 36 (92.3 %) were female, and 35/39 (89 %) were AQP4 Ab positive. Twelve patients were living with HIV. The most common clinical presentation was optic neuritis (38 %), followed by LETM (31 %). One or more relapses occurred in 24 patients (62 %). No significant risk factors for relapse were identified. Rituximab had the lowest relapse rate at 0.10 relapses per patient-year compared to azathioprine (0.23 relapses per patient-year) and mycophenolate mofetil (0.54 relapses per patient-year). No significant side effects were noted in people living with HIV and HIV negative patients using rituximab.

Conclusion: Chronic immunosuppression with rituximab was associated with the lowest relapse rate. In our population with a heavy burden of HIV, we have had no serious adverse events with using rituximab, which should be recommended as a first-line immunosuppressive agent in our setting.

1. Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disorder which involves the optic nerves, spinal cord, brainstem, and/or cerebrum. [1] In most cases, NMOSD is associated with antibodies directed against the Aquaporin 4 (AQP4) water channels found in astrocytes. [2] The binding of the AQP4 antibodies to the perivascular astrocytic podocytes leads to activation of the complement cascade and results in inflammation and tissue destruction with subsequent neurological deficits, depending on the region of the nervous system affected. [3] Clinical presentations include optic neuritis (ON), longitudinally extensive transverse myelitis (LETM), area postrema syndrome (APS), diencephalic syndrome and cerebral syndromes. [1]

Prevalence estimates vary considerably worldwide. A systematic review of NMOSD in Africa reported a prevalence of 0.052 per 100,000 in South Africa. [4] The impact of ethnicity on NMOSD is not clear, but there is a predilection toward non-white populations. [5] NMOSD occurs more commonly in females (9:1 female:male) with a median age of 39 years. [5] The presence of comorbid autoimmune diseases is found in 20–30 % of cases, including systemic lupus erythematosus, Sjogren's syndrome, coeliac disease, autoimmune hypothyroidism, myasthenia gravis and rheumatoid arthritis. [6] An association between tuberculosis and NMOSD has been reported in a previous study done in South Africa. [7]

NMOSD often has a relapsing clinical picture, with the risk of cumulative disability with each relapse. [8] Relapse rates range between

* Corresponding author.
E-mail address: jerry_1525@yahoo.com (J. George).

https://doi.org/10.1016/j.jns.2025.123589
Received 3 April 2025; Received in revised form 26 May 2025; Accepted 18 June 2025
Available online 19 June 2025
0022-510X/© 2025 Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

48 and 94 %, [9–11] with the average time to first relapse varying between 7 and 14 months. [12,13] Risk factors for relapse are not well understood but reportedly include female gender, younger age of onset, pregnancy and febrile illness. [14–16] Immunosuppressive treatment is used to prevent relapses and disease progression. The Food and Drug Administration-approved (FDA) immunosuppressive agents are inebilizumab, eculizumab and satralizumab. [17] These drugs are not available in the resource-constrained public healthcare sector in South Africa. Based on expert opinion and retrospective studies, azathioprine, mycophenolate mofetil (MMF) and rituximab have been recommended, with rituximab being documented to be the most effective. [18–21] Rituximab has been approved in Japan for NMOSD relapse prevention based on randomised controlled trial data. [22,23] However, in South Africa, a low-middle income country (LMIC), rituximab is not readily available and is inaccessible outside major centers. Furthermore, the safety profile of rituximab is unknown in a population with a high prevalence of HIV and tuberculosis, such as ours. [24]

We sought to describe the clinical profile and risk factors for relapse among NMOSD patients in South Africa and to compare relapse rates and adverse effects of the different immunosuppressive drugs available in our setting. Using this information, we aimed to motivate access to optimal disease-modifying therapy.

2. Methods

This prospective observational study was conducted in the three tertiary-level hospitals serving the population of Johannesburg, South Africa (Chris Hani Baragwanath Academic, Helen Joseph and Charlotte Maxeke Johannesburg Academic Hospitals) between January 2023 and June 2024. Johannesburg has a population of 5.5 million people, with an ethnicity distribution of 80.2 % Black African, 9.8 % Caucasian, 5.3 % Mixed Race, and 4.7 % Asian. [25] All patients aged 18 and older who met the 2015 NMOSD criteria were invited to participate. [1] Patients were invited to participate once the diagnosis of NMOSD was made either as an inpatient or at an outpatient neurology clinic in these three hospitals**.** This included newly diagnosed and previously diagnosed patients.

Data collected included demographics and co-morbidities (including autoimmune diseases such as systemic lupus erythematosus, type 1 diabetes mellitus, autoimmune vitamin B12 deficiency, HIV infection, and tuberculosis**).** Clinical characteristics, treatment regimens and relapses (defined as episodes of a new or objectively worsening neurological deficit lasting ≥24 h and occurring 30 days or more after the last attack) were also noted. Investigations performed included an autoimmune workup (Antinuclear antibody and Rheumatoid factor), Vitamin B12, glycated haemoglobin (HBA1C), erythrocyte sedimentation rate, angiotensin converting enzyme, Rapid Plasma Reagin, *Treponema Pallidum* Assay, lumbar puncture (cells, protein, glucose, Venereal Disease Research Laboratory Test, viral panel, GeneXpert, Cryptococcal Latex Agglutination Test), Aquaporin 4 antibody status (cell based assay) and anti-MOG antibody. Imaging included chest x-ray and MRI (brain and spine). Tuberculosis was screened for in all patients using a questionnaire [26] as well as chest Xray and abdominal sonar. In people living with HIV (PLWH), urine lipoarabinomannan was done**.** Side effects of long-term immunosuppressive therapy were documented. (Appendix A).

In the previously diagnosed patients, retrospective data was collected from hospital records and they were subsequently followed up for a minimum of 12 months. The newly diagnosed patients were also followed up for a minimum of 12 months**.** Informed consent was obtained from all participants, and their anonymity was maintained at all stages. Ethics approval was obtained from the management of all three hospitals and the University of the Witwatersrand Human Research Ethics Committee (Medical) (Clearance number M221144).

2.1. Data management and analysis

REDCap (Research Electric Data Capture) is a secure web-based data collection tool hosted by the University of the Witwatersrand. [27,28] A dedicated database was created for this study in 2023. Prospective data was collected over 12 months and combined with retrospective data of the previously diagnosed patients. Data was exported into Stata 18.0 (Stata Corporation, College Station, USA) for analysis. Descriptive statistics were used to document patients' demographic characteristics and treatment and treatment responses. Continuous variables were described using means and standard deviations if normally distributed or medians and interquartile ranges when non-normal. The Shapiro-Wilk test was used to assess normal distribution. Categorical variables were described as frequencies and percentages. A comparison of normally distributed continuous variables was made using the Student's *t*-test and non-normally distributed data using the rank sum test. The chi-squared test was used to compare categorical variables between male and female patients. *P*-values of 0.05 or less were regarded as significant.

3. Results

Altogether, 39 participants were recruited; 13 were newly diagnosed, and 26 were previously diagnosed. Demographic data are shown in Table 1. Twelve patients (30 %) were HIV positive, all were on antiretroviral therapy, and had a CD4 count >200 cells/μL. None of our patients had a simultaneous or preceding tuberculosis diagnosis.

The commonest clinical phenotype was optic neuritis, followed by LETM (Fig. 1).

3.1. Relapse precipitants and risk factors

Twenty-four patients (62 %) experienced one or more relapse episodes, resulting in a total of 41 relapse episodes over 123 patient-years. In 61 % of these episodes, no obvious relapse precipitant was identified. Pregnancy was the commonest identified relapse precipitant in 15 %. (Fig. 2).

Multivariate regression analyses, including gender, age, HIV status, presence of other autoimmune diseases and AQP4 Ab status, failed to identify any statistically significant risk factors for a relapse (Appendix B). Out of the 41 relapse episodes, 17 (41.5 %) occurred in spring, 13 (31.7 %) in summer, 6 (14.6 %) in autumn and 5 (12.2 %) in winter.

3.2. Long-term immunosuppressive therapy

Azathioprine was the most prescribed immunosuppressive agent (Table 2). Patients who relapsed on azathioprine were either maintained on azathioprine or escalated to either MMF or rituximab (Fig. 3). This decision was based on the opinion of the treating neurologist and the available resources at the time of relapse. Abnormal liver function was experienced by one patient on azathioprine, who was subsequently changed to another agent (Fig. 3).

MMF was used in nine patients, mainly as escalation therapy from azathioprine (Fig. 3). Patients who relapsed on MMF were escalated to rituximab. Rituximab was used in 12 patients, either as first-line (four patients), after relapsing on azathioprine or MMF (seven patients) and in

Table 1
Demographics ($n = 39$).

Variable	Frequency
Median age (years)	35 (IQR 28–45)
Female	36 (92.3 %)
Black African	39 (100 %)
People living with HIV	12 (30.8 %)
Other autoimmune diseases	5 (12.8 %)
AQP4* positive	35 (89.7 %)

* AQP4: aquaporin 4 antibody.

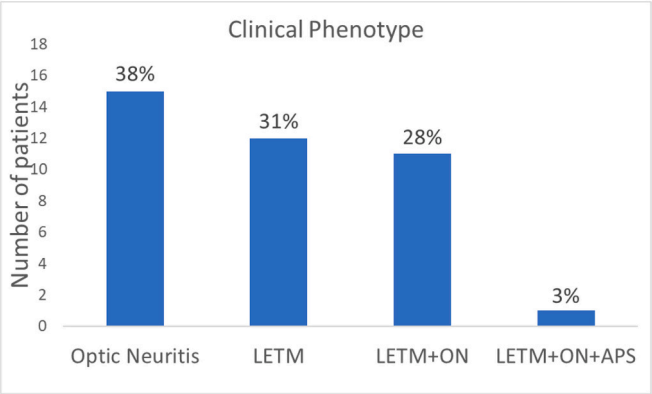

Fig. 1. Frequency of clinical phenotype of patients with neuromyelitis spectrum disorder.
APS: area postrema syndrome; LETM: longitudinally extensive transverse myelitis; ON: optic neuritis.

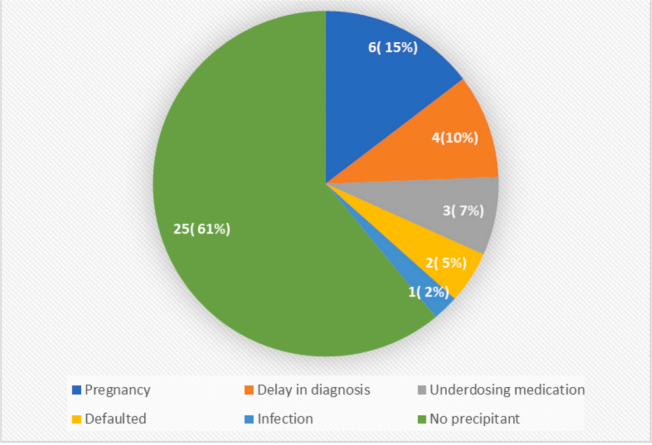

Fig. 2. Relapse precipitant for patients with NMOSD (41 relapse episodes).

Table 2
The immunosuppressive agents used and their respective relapse rates.

Agent	Number of patients	Patient-years	Number of relapses	Relapses per patient-year
Azathioprine	33	99	25	0.23
Mycophenolate mofetil	9	13	7*	0.54
Rituximab	12	11	1	0.10

* Includes one patient who had three relapses on MMF.

one patient who had a relapse after defaulting treatment (Fig. 3). One patient passed away from severe sepsis before long-term immunotherapy was initiated.

3.3. Relapses per agent

Rituximab had the lowest relapse rate (0.10 relapses per patient-year), followed by azathioprine (0.23 per patient-year) and MMF (0.54 per patient-year) (Table 2). However, of the nine patients on MMF, seven had been escalated from azathioprine with severe disease. When analysing only these seven patients, their relapse rates were similar on azathioprine (0.54 relapses per patient-year) and MMF (0.63 relapses per patient-year) (Table 3).

3.4. HIV

Twelve of the 39 patients (30 %) were people living with HIV (PLWH). Three of these patients had relapses (two were on azathioprine, and one defaulted MMF). The most prescribed agent in PLWH was azathioprine, which was used by eight patients. MMF was used by two participants (one after relapsing on azathioprine and the other as a first-line agent) and rituximab by five participants (used as first-line in three patients).

No significant adverse effects (infections, neutropenia) were noted when using these agents in this group (Appendix A). In our cohort, none of the patients developed tuberculosis as a complication of immunosuppression, and it was not a precipitant for developing NMOSD.

3.5. Comorbid autoimmune diseases

Five patients (13 %) had other comorbid autoimmune diseases: systemic lupus erythematosus [2], Type 1 diabetes mellitus [2] and pernicious anaemia [1]. The presence of comorbid autoimmune disease was not associated with an increased risk of relapse.

3.6. Side effects

One patient on azathioprine developed abnormal liver enzymes and was subsequently changed to MMF. One patient on MMF developed a urinary tract infection, and one patient receiving rituximab developed an infusion reaction (chills) on the first infusion. There was no neutropenia, thrombocytopenia or infections seen in patients using rituximab (HIV positive and negative).

4. Discussion

We describe a cohort of patients with highly active NMOSD, as evidenced by 24 of 39 patients experiencing relapses (62 % relapse rate). Our cohort was predominantly female (92 %) with a mean age of 35 years, similar to previously described data. [4,5] All our participants were black Africans. Comorbid HIV infection was seen in 30 % of our participants. This is less than that described in other South African literature, which showed 42–75 % of comorbid HIV. [7,29] The estimated prevalence of HIV in the adult population in South Africa is 19.6 %. [24] However, we do not have data on the prevalence of HIV in patients admitted to tertiary hospitals in South Africa.

The clinical phenotype in this cohort showed that the main presentation was ON, followed by LETM. This differs slightly from a 2021 systematic review of African studies which showed that LETM was more common than ON. [4] Our frequency of other autoimmune diseases (12 %) was lower than that reported in international literature, which estimated 20–30 % comorbid autoimmune disease. [6] There is a very high prevalence of tuberculosis in South Africa (737 per 100,000 people). [30] A possible association between tuberculosis and NMOSD has been described previously in South Africa. [7] However, none of the participants in our cohort had been diagnosed with tuberculosis before or after the diagnosis with NMOSD.

We report a relapse rate of 62 %, consistent with international literature. [9] Most relapses (61 %) had no identifiable precipitant; however, there was a delay in the diagnosis of NMOSD in four patients, resulting in relapses before immunosuppressive therapy was initiated. This calls for more aggressive education about NMOSD among healthcare workers and the public. Two of the 39 patients had defaulted treatment, and both developed relapses after seven and eight months, respectively. This highlights the severity of NMOSD and the need to counsel patients about the importance of adherence to chronic immunosuppressive medication, as relapses can be debilitating and cause considerable disability. We noted that most relapses occurred in summer, followed by spring. There is no clear explanation for this; however, it is similar to the findings of a case-controlled retrospective study

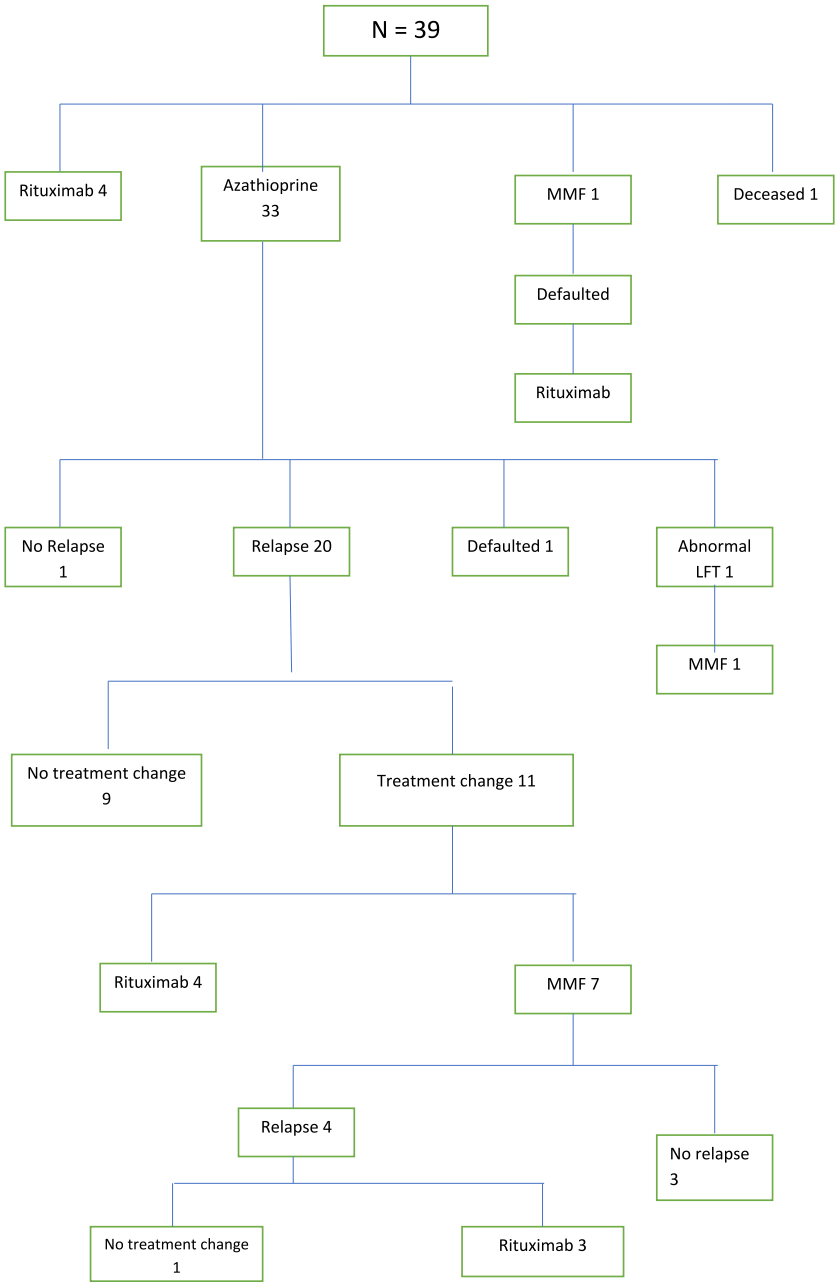

Fig. 3. Flow diagram of patients and their chronic immunosuppressive treatment. MMF: mycophenolate mofetil LFT: liver function test.

Table 3
Comparison of relapses of seven patients who changed to MMF whilst they were on azathioprine.

Agent	Number of patients	Patient-years	Relapses	Relapses per patient-year
Azathioprine	7	22	12	0.54
MMF	7	11	7	0.63

performed in New Zealand and Australia. [31]

Rituximab was the most effective of the long-term immunosuppressive therapies used in this cohort in preventing relapses, which is in keeping with international studies. [20,21] The only patient in our cohort who developed a relapse on rituximab had a particularly severe disease course. She had two relapses on azathioprine in one year and was then changed to MMF, on which she had three further relapses in 14 months. Once on rituximab, she developed a relapse in the fourth month of treatment and was relapse-free for the following 14 months. Our findings of azathioprine being slightly more efficacious than MMF differ from previous literature. [20,21] However, this apparent finding may partly be because of a single patient in our cohort who had three relapses on MMF, as well as the fact that MMF was used chiefly as escalation therapy after a patient relapsed on azathioprine.

In our resource-constrained setting, NMOSD patients are generally started on azathioprine, then changed to MMF after a relapse and only escalated to rituximab if they develop relapses on MMF. Our data confirms the evidence that rituximab is superior to azathioprine and MMF in decreasing relapse frequency and subsequent morbidity and mortality, though at a greater financial cost in the short term. [20,21] However, it is known that NMOSD relapses lead to cumulative morbidity and permanent disability. Thus, every possible effort should be undertaken to prevent relapses. In addition to the morbidity for the patient, more

relapses will make them heavily reliant on the healthcare and welfare systems for continuous support, thus drastically increasing the long-term cost per patient. This study was not designed to quantify such health economic implications. However, future studies are recommended which will potentially drive policy change to use drugs such as rituximab as first-line agents in NMOSD. Unfortunately, our study was unable to identify a particular subgroup of patients who were more prone to frequent and severe relapses. Identifying such risk factors in future studies could help select patients who would most benefit from rituximab.

There is little data on the safety of rituximab in PLWH with NMOSD. Some evidence suggests an increased risk of neutropenia, thrombocytopenia and infections, particularly in PLWH with CD4 counts <50cells/μL. [32] In a country like South Africa, with a high prevalence of HIV and tuberculosis, there is often hesitancy to use aggressive immunosuppressive therapy such as rituximab due to the possibility of infectious complications. [32,33] There were five PLWH on rituximab for a total of 4.5 patient-years in our cohort. No serious adverse effects were noted in these patients (including sepsis or neutropenia). One patient developed infusion-related chills during the first infusion. None of these patients had a relapse. This provides some reassurance that the added efficacy does not appear to come with any additional adverse effects.

4.1. Limitations

The limitations of our study include the fact that some of the data was retrospective. The choice of chronic immunosuppression was based on the assessment of the treating neurologist and the availability of the immunosuppressive agents at that time, and not on a standardised protocol. Our sample size, albeit small, is one of the largest from our region.

5. Conclusion

We describe a cohort of 39 patients with highly active NMOSD. Rituximab was associated with the lowest relapse rate compared to azathioprine and MMF. We have shown that rituximab can be used safely in a population with a high prevalence of HIV and tuberculosis and should thus be considered as first-line immunosuppression for patients with NMOSD in our setting.

CRediT authorship contribution statement

Jerry George: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Eitzaz Sadiq:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization. **Andre Mochan:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

Ethics approval

Ethics approval was granted by the University of the Witwatersrand Human Research Ethics Committee (Medical) (Certificate M221144).

Funding

None.

Declaration of competing interest

None.

Appendix A. Appendix

A.1. Side effects monitored for long-term immunosuppression

A.1.1. Rituximab

Infusion-related side effects (hives, itching, swelling lips, palpitations, dizziness)
Infections (progressive multifocal leukoencephalopathy)
Persistent leukopenia

A.1.2. Mycophenolate mofetil

The principal side effects monitored included diarrhoea, sepsis, vomiting, leukopenia and opportunistic infections

A.1.3. Azathioprine

Side effects monitored in patients using azathioprine include nausea, fever, vomiting, hepatotoxicity, leukopenia and bone marrow suppression.

A.2. Side effects noted

A.2.1. Rituximab

Infusion-related chills

A.2.2. Mycophenolate mofetil

Urinary tract infection (one patient)

A.2.3. Azathioprine

Hepatotoxicity (one patient)

Appendix B. Appendix

B.1. Risk factors for relapse among patients with NMO

Variable	% with ≥ 1 relapses	Prevalence rate ratio (PRR), 95 %CI	p-value	Adjusted prevalence rate ratio (aPRR) 95 %CI	p-value
Age in years		0.97 (0.95–0.99)	0.016	0.98 (0.96–1.00)	0.111
Sex					
Female	22/36 (61.1)	1.00		–	–
Male	2/3 (66.7)	1.09 (0.47–2.56)	0.841		
People living with HIV			0.155	–	–
No	19/27 (70.4)	1.67 (0.82–3.48)			
Yes	5/12 (41.7)	1.00			
Autoimmune diseases				–	–
No	20/34 (58.8)	1.00	0.253		
Yes	4/5 (80.0)	1.36 (0.80–2.30)			
More than one NMOSD phenotype	9/20 (45.0)	1.00		1.00	
No	15/19 (79.0)	1.75 (1.02–3.02)	0.042	1.55 (0.95–2.50)	0.077
Yes					
Season of diagnosis				–	–
Summer	14/21(66.7)	1.5 (0.67–3.34)	0.321		
Autumn	1/1 (100)	2.25 (1.07–4.02)	0.032		
Winter	5/7 (71.4)	1.61 (0.67–3.87)	0.292		
Spring	4/9 (44.4)	1.00			
AQP4 status				–	–
Negative	3 /4 (75.0)	1.25 (0.66–2.36)	0.491		
Positive	21/35 (60.0)	1.00			

Legend
APS: area postrema syndrome
AQP4 Ab: aquaporin 4 antibody
CD4: Cluster of differentiation 4
FDA: Food and Drug Administration
HIV: human immunodeficiency virus
LETM: longitudinally extensive transverse myelitis
LFT: liver function test
LMIC: low- and middle-income countries
MMF: mycophenolate mofetil
NMOSD: neuromyelitis optica spectrum disorders
ON: optic neuritis
PLWH: people living with HIV
REDCap: Research Electronic Data Capture
USA: United States of America

Data availability

All data will be available to qualified researchers upon reasonable request.

References

[1] D.M. Wingerchuk, B. Banwell, J.L. Bennett, P. Cabre, W. Carroll, T. Chitnis, et al., International consensus diagnostic criteria for neuromyelitis optica spectrum disorders, Neurology 85 (2) (2015) 177–189.
[2] V.A. Lennon, T.J. Kryzer, S.J. Pittock, A.S. Verkman, S.R. Hinson, IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel, J. Exp. Med. 202 (4) (2005) 473–477.
[3] D.M. Wingerchuk, V.A. Lennon, C.F. Lucchinetti, S.J. Pittock, B.G. Weinshenker, The spectrum of neuromyelitis optica, Lancet Neurol. 6 (9) (2007) 805–815.
[4] A.K. Musubire, J. Derdelinckx, T. Reynders, D.B. Meya, P.R. Bohjanen, P. Cras, et al., Neuromyelitis optica spectrum disorders in Africa: a systematic review, Neurol Neuroimmunol. Neuroinflamm. 8 (6) (2021).
[5] M. Etemadifar, Z. Nasr, B. Khalili, M. Taherioun, R. Vosoughi, Epidemiology of neuromyelitis optica in the world: a systematic review and meta-analysis, Mult. Scler. Int. 2015 (2015) 174720.
[6] A. Iyer, L. Elsone, R. Appleton, A. Jacob, A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitis optica, Autoimmunity 47 (3) (2014) 154–161.
[7] V. Zatjirua, J. Butler, J. Carr, F. Henning, Neuromyelitis optica and pulmonary tuberculosis: a case-control study, Int. J. Tuberc. Lung Dis. 15 (12) (2011) 1675–1680.
[8] A. Berthele, M. Levy, D.M. Wingerchuk, S.J. Pittock, S. Shang, A. Kielhorn, et al., A single relapse induces worsening of disability and health-related quality of life in patients with neuromyelitis optica spectrum disorder, Front. Neurol. 14 (2023) 1099376.
[9] D.M. Wingerchuk, W.F. Hogancamp, P.C. O'Brien, B.G. Weinshenker, The clinical course of neuromyelitis optica (Devic's syndrome), Neurology 53 (5) (1999) 1107.
[10] M.A. Mealy, D.M. Wingerchuk, B.M. Greenberg, M. Levy, Epidemiology of neuromyelitis optica in the United States: a multicenter analysis, Arch. Neurol. 69 (9) (2012) 1176–1180.
[11] M. Royston, A. Kielhorn, D. Weycker, M. Shaff, L. Houde, I. Tanvir, et al., Neuromyelitis Optica Spectrum disorder: clinical burden and cost of relapses and disease-related care in US clinical practice, Neurol. Ther. 10 (2) (2021) 767–783.
[12] J. ZhangBao, L. Zhou, X. Li, T. Cai, J. Lu, C. Lu, et al., The clinical characteristics of AQP4 antibody positive NMO/SD in a large cohort of Chinese Han patients, J. Neuroimmunol. 302 (2017) 49–55.
[13] J. Kitley, M.I. Leite, I. Nakashima, P. Waters, B. McNeillis, R. Brown, et al., Prognostic factors and disease course in aquaporin-4 antibody-positive patients with neuromyelitis optica spectrum disorder from the United Kingdom and Japan, Brain 135 (6) (2012) 1834–1849.
[14] X. Ma, A.G. Kermode, X. Hu, W. Qiu, Risk of relapse in patients with neuromyelitis optica spectrum disorder: recognition and preventive strategy, Mult. Scler. Relat. Disord. 46 (2020) 102522.
[15] Y. Huang, Y. Wang, Y. Zhou, Q. Huang, X. Sun, C. Chen, et al., Pregnancy in neuromyelitis optica spectrum disorder: a multicenter study from South China, J. Neurol. Sci. 372 (2017) 152–156.
[16] V.T.W. Chang, H.M. Chang, Review: recent advances in the understanding of the pathophysiology of neuromyelitis optica spectrum disorder, Neuropathol. Appl. Neurobiol. 46 (3) (2020) 199–218.
[17] F. Held, A.-K. Klein, A. Berthele, Drug treatment of neuromyelitis optica spectrum disorders: out with the old, in with the new? Immuno.Targets Ther. 10 (2021) 87–101.
[18] D.J. Kimbrough, K. Fujihara, A. Jacob, M.A. Lana-Peixoto, M.I. Leite, M. Levy, et al., Treatment of neuromyelitis optica: review and recommendations, Mult. Scler. Relat. Disord. 1 (4) (2012) 180–187.
[19] R.A. Kessler, M.A. Mealy, M. Levy, Treatment of neuromyelitis optica spectrum disorder: acute, preventive and symptomatic, Curr. Treat. Options Neurol. 18 (1) (2016) 2.
[20] I.H. Jeong, B. Park, S.H. Kim, J.W. Hyun, J. Joo, H.J. Kim, Comparative analysis of treatment outcomes in patients with neuromyelitis optica spectrum disorder using multifaceted endpoints, Mult. Scler. 22 (3) (2016) 329–339.

[21] M.A. Mealy, D.M. Wingerchuk, J. Palace, B.M. Greenberg, M. Levy, Comparison of relapse and treatment failure rates among patients with neuromyelitis optica: Multicenter study of treatment efficacy, JAMA Neurol. 71 (3) (2014) 324–330.
[22] T. Kümpfel, K. Giglhuber, O. Aktas, I. Ayzenberg, J. Bellmann-Strobl, V. Häußler, et al., Update on the diagnosis and treatment of neuromyelitis optica spectrum disorders (NMOSD) – revised recommendations of the neuromyelitis optica study group (NEMOS). Part II: attack therapy and long-term management, J. Neurol. 271 (1) (2024) 141–176.
[23] M. Tahara, T. Oeda, K. Okada, T. Kiriyama, K. Ochi, H. Maruyama, et al., Safety and efficacy of rituximab in neuromyelitis optica spectrum disorders (RIN-1 study): a multicentre, randomised, double-blind, placebo-controlled trial, Lancet Neurol. 19 (4) (2020) 298–306.
[24] South African Government, People of South Africa: SA gov, Last accessed 20 March 2025 [Available from: https://www.gov.za/about-sa/people-south-africa-0#:~:text=The%20estimated%20overall%20HIV%20prevalence, 2022. ,the% 20population%20is%20HIV%20positive.
[25] South African Government, City of Johannesburg, in: Coorperative Governance anf Traditional Affairs, Editor, 2020, p. 13. Johannesburg.
[26] Department Health RoSA, TB Screening Andtesting, Standard Operating Procedure, 1112 Voortrekker Rd, Pretoria Townlands 351-JR, Pretoria, May 2023, pp. 12–13.
[27] P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support, J. Biomed. Inform. 42 (2) (2009) 377–381.
[28] P.A. Harris, R. Taylor, B.L. Minor, V. Elliott, M. Fernandez, L. O'Neal, et al., The REDCap consortium: building an international community of software platform partners, J. Biomed. Inform. 95 (2019) 103208.
[29] A.I. Bhigjee, A.A. Moodley, I. Roos, C.L. Wells, P. Ramdial, M. Esser, The neuromyelitis optica presentation and the aquaporin-4 antibody in HIV-seropositive and seronegative patients in KwaZulu-Natal, South Africa, South Afr. J. HIV Med. 18 (1) (2017) 684.
[30] Department Health RoSA, The First National TB Prevalence Survey, South Africa, Pretoria, 2018.
[31] E. Khalilidehkordi, L. Clarke, S. Arnett, W. Bukhari, S. Jimenez Sanchez, C. O'Gorman, et al., Relapse patterns in NMOSD: evidence for earlier occurrence of optic neuritis and possible seasonal variation, Front. Neurol. 11 (2020).
[32] M. Spina, U. Tirelli, Rituximab for HIV-associated lymphoma: weighing the benefits and risks, Curr. Opin. Oncol. 17 (5) (2005) 462–465.
[33] E. Ghrenassia, E. Mariotte, E. Azoulay, Rituximab-Related Severe Toxicity, Springer International Publishing, 2018, pp. 579–596.